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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,534	02/20/2004	David Alan Mead	MICRO-08797	7480

7590 08/09/2005

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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/783,534	MEAD ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 29-41 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 29-41 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 20 February 2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/16/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 20 February 2004, which is a continuation of application 10/740,714 filed 19 December 2003, which is a continuation of application 10/001,052 filed 15 November 2001, which claims benefit of provisional application 60/249;594 filed 17 November 2000. The preliminary amendments filed 20 February 2004 and 2 August 2004 have been entered. Claims 1-28 were originally filed. Claims 1-28 were canceled and claims 29-41 were added in the 20 February amendment. Claims 29-41 are pending and under consideration.

Specification

Amendment of the specification to indicate the claimed priority in the amendment filed 20 February 2004 is acknowledged. It is noted that the priority claim does not include the current status of the 10/001,052 application, which is now Patent No 6,709,861. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included in the priority claim. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are directed to a circular vector comprising a nucleic acid sequence comprising first and second ends and various elements positioned relative to said first and second ends. However, there is nothing in the claim that fixes the position of the first and second ends within the nucleic acid sequence. In other words, according to the broadest reasonable interpretation of the claim, the first and second ends can be anywhere within the nucleic acid sequence. According to this interpretation, the second and third transcriptional terminators might lie anywhere within the boundaries of the "nucleic acid sequence" portion of the circular vector. However, an alternative interpretation of the claim is that the first and second ends define the boundaries of the sequence comprising elements ii), iii) and iv) of the nucleic acid sequence and that the transcriptional terminators lie outside of boundaries of the "nucleic acid sequence". As these alternative interpretations result in a significant difference scope of the subject matter encompassed by the claims, the metes and bounds of the claims as a whole are of indefinite. Applicant is urged to amend the claims to clearly define the position of the "first and second ends" while being careful not to introduce new matter into the claims.

Claims 32 and 38 are further indefinite in reciting that the selectable marker region comprises "first and second selectable marker sequences". It is unclear what distinguishes the first selectable marker sequence from the second selectable marker sequence. For example, are nucleic acids encoding two distinct domains of a single selectable marker protein first and second selectable marker sequences or must the first and second selectable marker sequences

encode distinct selectable markers? As it is unclear what defines and distinguishes a first selectable marker sequence from a second selectable marker sequence, the metes and bounds of the claims are unclear. In the interest of advancing prosecution, the indefinite limitation will be construed according the broadest reasonable interpretation of the claim. Therefore, "first and second selectable marker sequences" is understood to encompass any two distinct nucleic acid sequences within a region that comprises the selectable marker.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen *et al.* (1987) *Gene* 55:179-187 (made of record in the IDS filed 16 August 2004) as evidenced by Kobayashi *et al.* (1986) *J. Bacteriol.* 166:728-732 and Altieri *et al.* (1986) *J. Bacteriol.* 168:648-654.

The claims are directed to a circular vector comprising: a toxic gene sequence; a nucleic acid sequence comprising first and second ends, a selectable marker region an origin of replication and a first transcriptional terminator downstream of said selectable marker region; a second transcriptional terminator between said toxic gene sequence and said first end; and a third transcriptional terminator between said toxic gene sequence and said second end.

In Figure 2, Chen *et al.* teaches a circular vector (pJDC9) comprising, recited in clockwise order, a lacZ selectable marker, a transcriptional terminator downstream of the lacZ gene, the pMB9 plasmid, and tandem T_2T_1 transcriptional terminators. Kobayashi *et al.* teaches that pMB9 plasmid comprises the *kil* gene, the expression of which is known to cause cell lysis (see especially the second paragraph on page 728 and the final paragraph on page 731). Thus, the pJDC9 plasmid of Chen *et al.* comprises a toxic *kil* gene within the pMB9 plasmid portion. As discussed above, the position of the first and second ends is construed as being anywhere within the "nucleic acid sequence".

Thus, the circular vector of Chen *et al.* comprises a toxic gene sequence and a "nucleic acid sequence" comprising a selectable marker region, an origin of replication (as evidenced by the ability of the vector to be propagated in host cells). Furthermore, the vector of Chen *et al.* comprises second and third transcriptional terminators, which, based on the arbitrary nature of the "first and second ends" of the claims, are construed as being positioned between the first and/or second ends and the toxic gene sequence. Therefore, the circular vector of Chen *et al.* comprises all of the elements of the vector of the instant claim 29.

Furthermore, the first transcriptional terminator in the vector of Chen *et al.* is configured to terminate RNA transcripts encoded by the selectable marker according to the instant claim 30; given the arbitrary nature of the first and second ends and the broad scope of non-promoter sequence (*i.e.*, any sequence that does not comprise all of the elements necessary to operate as a promoter), the vector of Chen *et al.* comprises non-promoter sequence positioned as recited in claim 31; and, likewise, as any nucleic acid sequence can serve as a primer binding site, the vector of Chen *et al.* comprises two primer binding sites according to the limitations of claim 33.

Claim 32 recites that the selectable marker region comprises first and second selectable marker sequences, which is indefinite (*Id.*). However, given the broadest reasonable interpretation of the claim, the selectable marker sequences (*i.e.*, portions of the lacZ gene) distinguished by lying on either side of the MCS in the vector of Chen *et al.* meet the limitation of first and second selectable marker sequences.

Claim 34 recites that the toxic gene, when expressed, is configured to prevent growth of a cell. Altieri *et al.* teaches that the *kil* gene comprised by the circular vector of Chen *et al.*, when expressed, has the ability to prevent growth of a host cell according to the limitations of claim 34 (see especially the second paragraph on page 648 and the section entitled "Expression of the *kil* gene in pUKIL" beginning on page 649, particularly the final paragraph on page 649).

Thus, the circular vector of Chen *et al.*, as evidenced by Kobayashi *et al.* and Altieri *et al.*, comprises each of the elements of the circular vector of the instant claims. Therefore, the claims are anticipated by Chen *et al.* as evidenced by Kobayashi *et al.* and Altieri *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen *et al.* (*supra*) as evidenced by Kobayashi *et al.* (*supra*) and Altieri *et al.* (*supra*) in view of "Directional Cloning" *in* Molecular Cloning, a laboratory manual (Maniatis *et al.*, Eds.) Cold Spring Harbor Laboratory, 1982, pp. 13 (hereinafter, Maniatis *et al.*).

The claims are directed to a method of forming a vector component comprising providing a composition comprising a first circular vector having the structural properties of the vector of claim 29 (*Id.*) and further comprising a first restriction enzyme recognition site between the toxic gene sequence and the second transcriptional terminator and a second restriction enzyme recognition site between the toxic gene sequence and the third transcriptional terminator. The method further comprises mixing the composition with one or more restriction enzymes such that the first circular vector is cleaved at the first and second restriction enzyme recognition sites, thereby generating a vector component with first and second free ends.

As described above, Chen *et al.* as evidenced by Kobayashi *et al.* and Altieri *et al.* teach a composition comprising all of the elements of the vector of claim 29. Furthermore, the vector of Chen *et al.* comprises a multiple cloning site in the lacZ gene, which comprises first and second restriction enzyme recognition sites. When read in the clockwise direction, the restriction sites are positioned between the second and third transcriptional terminators (*i.e.*, tandem T_2T_1 terminators) and the toxic gene sequence in the pMB9 plasmid element (see especially Figure 2, pJDC9).

Chen *et al.* further teaches a method of cloning *pneumococcal* DNA into pJDC9 comprising digesting the circular vector with HindIII (see especially the paragraph bridging pages 185-186, TABLE III and the legend thereto). Thus, Chen *et al.* teaches a method comprising all of the process steps of the instant claim 35 except for the cleavage at a second restriction enzyme recognition site.

Maniatis *et al.* teach that the efficiency of cloning in plasmid vectors comprising multiple restriction enzyme recognition sites can be enhanced by digesting with two enzymes that leave non-compatible termini.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the cloning method of Chen *et al.* to including digestion of a second restriction enzyme recognition site present in the multiple cloning site of pJDC9 according to the limitations of the instant claims. Motivation to combine the teachings comes from the nature of the problem to be solved in the method of method of Chen *et al.*, which is to clone *pneumococcal* genomic DNA, and the teachings of Maniatis *et al.* stating that efficiency of cloning can be enhanced by the generation of non-complementary vector termini. Absent evidence to the

contrary, one would have a reasonable expectation of success in combining these teachings in view of the well-established and routine nature of directional cloning in plasmid vectors.

For these reasons, the method of claim 35, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Furthermore, as claims 36-40 merely recite structural limitations present in the vector of Chen *et al.* (see, *supra*; the limitations of claims 36-40 correspond to claims 30-34, respectively), the claims are also obvious over the art for the reasons set forth herein above.

Finally, claim 41 is directed to the method further comprising mixing said vector component with a library of insert sequences under conditions such that a second circular vector, comprising at least one insert sequence, is generated. As the method of cloning *pneumococcal* DNA of Chen *et al.* further comprises ligation of said *pneumococcal* DNA with the digested pJDC9 vector (see especially Table III and the legend thereto), the method of claim 41, as a whole, would also have been obvious to one of ordinary skill in the art in view of the teachings of the cited art for the reasons set forth herein above.

For these reasons, the claimed invention, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC §103(a).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER